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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/287,248	04/07/1999	JOHN T. MCDEVITT	5119-00501	6075

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EXAMINER	
PADMANABHAN, KARTIC	23

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 03/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/287,248	MCDEVITT ET AL.	
	Examiner	Art Unit	
	Kartic Padmanabhan	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36,39,173 and 174* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-36,39,173 and 174* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 April 1999* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *21* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. Claims 1-19, 39, and 173 are rejected under 35 U.S.C. 102(e) as being anticipated by Stabile et al. (US Pat. 5,872,623). Stabile et al. disclose a detection device comprising a light source that is reflected onto a clear lens above the sensor array. The light source is a light emitting diode (Col. 3, lines 32-33). The device also comprises a planar substrate support and sensor array. The sensor array comprises top and bottom layers, as well as cavities in which a plurality of particles may be positioned. These particles are able to produce a signal or swell when the particles interact with analyte. The particles may be between 100 and 200 um in diameter (Col. 15). The support material may be made of glass, fused silica, silicon wafer, or plastic. The support surface may be treated with a siliconizing agent that minimizes the reactive sites that bind biological molecules. A detector, either a charge coupled device, photodiode array, or photodetector, is positioned beneath the apparatus for detecting the signal produced by the interaction of the analyte with article(s) during use. The reference also discloses a liquid distribution system that is coupled to the device and delivers fluid from different reservoirs to the reaction cells or detection sites (Col. 13).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stabile et al. (US Pat. 5,872,623) in view of Ito et al. (US Pat. 5,583,054).

Stabile et al. teach a detection system, as previously discussed. However, the reference does not teach particles containing metal oxide.

Ito et al. teach reagent particles containing metal oxide as magnetic material. These particles provide the advantage of no residual magnetization (Col. 4, line 30). The reagent particles support immobilized antibodies on their surface (Col. 4, lines 6-16).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the device of Stabile et al. by substituting particles containing metal oxide as taught by Ito et al. because metal oxide particles are known solid supports for supporting immunoreagents in assays for analyte detection and thus an obvious alternative to the particles taught by the Stabile reference. One would have had a reasonable expectation of success in using the metal oxide particles of Ito et al. with the device of Stabile et al.

7. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stabile et al. (US Pat. 5,872,623) in view of Colin et al. (US Pat. 5,773,307).

Stabile et al. teach a detection system, as previously discussed. However, the reference does not teach metal particles.

Colin et al. teach a primary reagent used in analyte detection that consists of metal particles in a suspension consisting of at least one anti-ligand fixed to the surface of the particle (Col. 2, lines 25-35).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the device of Stabile et al. by substituting metal particles as taught by Colin et al. because metal particles are known solid supports for supporting immunoreagents in assays for analyte detection and thus an obvious alternative to the particles taught by the Stabile reference. One would have had a reasonable expectation of success in using the metal particles of Colin et al. with the device of Stabile et al.

8. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stabile et al. (US Pat. 5,872,623) in view of Clark Jr. et al. (US Pat. 5,690,807).

Stabile et al. teach a detection system, as previously discussed. However, the reference does not teach semiconductor particles.

Clark Jr. et al. teach a method for producing semiconductor particles. Particles ranging from 1-1000 nm are useful for their quantum confinement effects and their luminescent properties (Col. 1, lines 18-21).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the device of Stabile et al. by substituting semiconductor particles as taught by Clark Jr. et al. because semiconductor particles are known solid supports for supporting immunoreagents in assays for analyte detection and thus an obvious alternative to the particles taught by the Stabile reference. In addition, these particles provide the advantage of quantum confinement and luminescent properties. The luminescent properties of the particles of Clark Jr. et al. obviate the need for a separate labeling step to generate an optical signal. One would have had a reasonable expectation of success in using the semiconductor particles of Clark Jr. et al. with the device of Stabile et al.

9. Claims 23-24 and 174 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stabile et al. (US Pat. 5,872,623) in view of McGarry et al. (US Pat. 5,248,742).

Stabile et al. teach a detection system, as previously discussed. However, the reference does not teach a polymeric resin.

McGarry et al. teach various vinyl crosslinkers, such as divinyl benzene, utilized in the formation of polymeric resins.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the device of Stabile et al. by using polymeric resin particles substituted with a crosslinker such as divinyl benzene. One would have been motivated to do so because polymeric resin beads are well known solid supports for supporting immunoreagents in assays for analyte detection and thus an obvious alternative to the particles taught by the Stabile reference. In addition, the addition of the crosslinking agent merely represent an optimization of the device, since agents such as divinyl benzenes are conventional monomers used in the production of polymeric beads.

10. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stabile et al. (US Pat. 5,872,623) in view of McGarry et al. (US Pat. 5,248,742) as applied to claims 23-24 and 174 above and further in view of Bretscher et al. (US Pat. 5,714,122).

Stabile et al. and McGarry et al. teach a modified detection system, as previously discussed. However, the references do not teach a receptor that produces a signal in response to the pH of a fluid.

Bretscher et al. teach pH sensitive optical indicators used in the detection of carbon dioxide in blood. The pH change can be monitored by fluorescence or absorption (Col. 7, lines 56-66).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the device of Stabile et al. and McGarry et al. by incorporating a dye as taught by Bretscher et al. because the dye of Bretscher et al. may be incorporated into a particle as a receptor and used in the modified device of Stabile et al. and McGarry et al. to detect pH changes in a sample medium. The analyte or parameter to be detected dictates the reagents to be

used in an assay, and selection of these simply represent an optimization of the device assay, depending on what one wishes to assay.

11. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stabile et al. (US Pat. 5,872,623) in view of McGarry et al. (US Pat. 5,248,742) as applied to claims 23-24 and 174 above and further in view of Arnold et al. (US Pat. 5,616,790).

Stabile et al. and McGarry et al. teach a modified detection system, as previously discussed. However, the references do not teach a receptor producing a signal in the presence of a metal ion.

Arnold et al. teach a fluorescent metal-chelating amphiphile used as a sensor for the detection of metal ions in solution. The disclosed amphiphile is placed in a lipid bilayer or other suitable matrix. The resulting mixed lipid bilayer system functions as a sensor for metal ions (Col. 4, lines 1-41).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the device of Stabile et al. and McGarry et al. by using the amphiphile of Arnold et al. as the receptor because the amphiphile of Arnold et al. forms aggregates when placed in a lipid bilayer to detect metal ions. Once again, since the desired analyte to be detected dictates the selection of reagents (receptor in this case), the selection of the receptor simply represents an optimization of the assay, and one of skill in the art would have had a reasonable expectation of success in making this optimization with the modified device of Stabile and McGarry et al.

12. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stabile et al. (US Pat. 5,872,623) in view of McGarry et al. (US Pat. 5,248,742) as applied to claims 23-24 and 174 above and further in view of Russell (US Pat. 5,137,833).

Stabile et al. and McGarry et al. teach a modified detection system, as previously discussed. However, the references do not teach a receptor for carbohydrates.

Russell teaches a class of dyes that exhibit quantitative sensitivity to the presence of certain polyhydroxyl compounds, such as sugars. The dye is bound to a derivative of boronic, arsenious, or germanic acid. The simplest detection system comprises a sample carrier, a light source or source of radiation, and a detector capable of measuring the intensity of radiation passing through the sample (Col. 2).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the device of Stabile et al. and McGarry et al. by using a receptor comprising a dye and a derivative of boronic acid, as taught by Russell. The selection of specific receptors simply represents an optimization of the device and does not patentably distinguish the present invention over the prior art. Depending on the analyte to be detected, one of skill in the art would have known to use a receptor for that specific analyte. In addition, Russell teaches that their dye reagents can be used in optical devices, which would allow one to use the modified device of Stabile et al. and McGarry et al. with the dyes of Russell with a reasonable expectation of success.

13. Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stabile et al. (US Pat. 5,872,623) in view of McGarry et al. (US Pat. 5,248,742) as applied to claims 23-24 and 174 above and further in view of Schutz et al. (Biophysical Journal, 1998).

Stabile et al. and McGarry et al. teach a modified detection system, as previously discussed. However, the references do not teach colocalization of indicators on the receptor.

Schutz et al. teach colocalization of two types of ligands on a receptor to be used in fluorescence microscopy (page 2223). Observation of emission from an acceptor molecule during illumination of a donor allows the testing for energy transfer (page 2225).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the device of Stabile et al. and McGarry et al. by using a receptor comprising colocalized ligand indicators as taught by Schutz et al. because such a configuration may be incorporated onto a particle and provides the advantage of high sensitivity in the optical detection systems.

14. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stabile et al. (US Pat. 5,872,623) in view of McGarry et al. (US Pat. 5,248,742) as applied to claims 23-24 and 174 above and further in view of Issachar et al. (US Pat. 5,156,972).

Stabile et al. and McGarry et al. teach a modified detection system, as previously discussed. However, the references do not teach an indicator associated with a receptor such that the indicator is displaced in the presence of analyte.

Issachar et al. teach biosensors in which immobilized receptors and ligands are connected together on a solid phase on the absence of analyte. In analyte presence, ligand is displaced from the receptor to produce a signal (Col. 6, lines 29-39).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the device of Stabile et al. and McGarry et al. by using a receptor-ligand moiety for signal detection of an analyte by displacement of the ligand from the receptor in analyte presence as taught by Issachar et al. because Issachar et al. show it to be conventional in the art to perform displacement immunoassays with optical devices.

15. Claims 30 and 35-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stabile et al. (US Pat. 5,872,623) in view of McGarry et al. (US Pat. 5,248,742) as applied to claims 23-24 and 174 above and further in view of Fish et al. (US Pat. 5,126,276).

Stabile et al. and McGarry et al. teach a modified detection system, as previously discussed. However, the references do not teach different types of receptors.

Fish et al. teach receptors that are selectively attached onto supports with the type of receptor varying with the analyte to be assayed. Examples of receptors include antigens, antibodies, and nucleic acids (Col. 7, lines 54-62).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the device of Stabile et al. and McGarry et al. by using the various receptors taught by Fish et al. because the choice of receptors represent a mere optimization of the device. Depending on the analyte to be assayed, one would have had a reasonable expectation of success in selecting any number of receptors for use with the modified device of Stabile et al. and McGarry et al.

16. Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stabile et al. (US Pat. 5,872,623) in view of McGarry et al. (US Pat. 5,248,742) as applied to claims 23-24 and 174 above and further in view of Lauritzen (Electrophoresis, 1993).

Stabile et al. and McGarry et al. teach a modified detection system, as previously discussed. However, the references do not teach a peptide receptor.

Lauritzen teaches a peptide receptor immobilized on a solid substrate for antibody binding.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the device of Stabile et al. and McGarry et al. by using the peptide

receptor taught by Lauritzen because the choice of receptors represent a mere optimization of the device. Depending on the analyte to be assayed, one would have had a reasonable expectation of success in selecting any number of receptors for use with the modified device of Stabile et al. and McGarry et al.

17. Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stabile et al. (US Pat. 5,872,623) in view of McGarry et al. (US Pat. 5,248,742) as applied to claims 23-24 and 174 above and further in view of Khanna et al. (US Pat. 5,223,393).

Stabile et al. and McGarry et al. teach a modified detection system, as previously discussed. However, the references do not teach an enzyme receptor.

Khanna et al. teach an enzyme immunoassay in which an enzyme receptor is used for analyte detection (Col. 3, lines 17-36). The enzyme receptor can be used to detect polypeptides, proteins, nucleic acids, polysaccharide, etc. (Col. 4, lines 46-51).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the device of Stabile et al. and McGarry et al. by using the enzyme receptor taught by Khanna et al. because the choice of receptors represent a mere optimization of the device. Depending on the analyte to be assayed, one would have had a reasonable expectation of success in selecting any number of receptors for use with the modified device of Stabile et al. and McGarry et al. In addition, the use of an enzyme receptor on beads for analyte detection is well known and conventional in the art.

18. Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stabile et al. (US Pat. 5,872,623) in view of McGarry et al. (US Pat. 5,248,742) as applied to claims 23-24 and 174 above and further in view of O'Daly et al. (US Pat. 5,391,272).

Stabile et al. and McGarry et al. teach a modified detection system, as previously

discussed. However, the references do not teach a synthetic receptor.

O'Daly et al. teach an example of a different type of binding entity such as a synthetic receptor to which a ligand or cross-reacting compound binds (Col. 6, lines 39-44).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the device of Stabile et al. and McGarry et al. by using the synthetic receptor taught by O'Daly et al. because the choice of receptors represent a mere optimization of the device. Depending on the analyte to be assayed, one would have had a reasonable expectation of success in selecting any number of receptors for use with the modified device of Stabile et al. and McGarry et al. In addition, O'Daly et al. show it to be conventional in the art to use synthetic receptors in solid phase immunoassays.

19. Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stabile et al. (US Pat. 5,872,623) in view of McGarry et al. (US Pat. 5,248,742) as applied to claims 23-24 and 174 above and further in view of Cho et al. (Science, 1993).

Stabile et al. and McGarry et al. teach a modified detection system, as previously discussed. However, the references do not teach an unnatural biopolymer receptor.

Cho et al. teach the synthesis of unnatural biopolymers composed of building blocks other than amino acids. These biopolymers are used as a screening tool for their ability to function as receptors for monoclonal antibodies (page 1303).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the device of Stabile et al. and McGarry et al. by using the unnatural biopolymer receptor taught by Cho et al. because these receptors are commercially available, and the choice of receptors represent a mere optimization of the device. Depending on the analyte to

be assayed, one would have had a reasonable expectation of success in selecting any number of receptors for use with the modified device of Stabile et al. and McGarry et al. .

Response to Arguments

20. Applicant's arguments filed 12/23/02 have been fully considered but they are not persuasive to overcome the Stabile reference and all rejections on which this reference is relied upon.

21. Applicant's argument that the Stabile reference does not teach the cover layer at a distance above the supporting member such that dislodgement of particles is inhibited is erroneous. Given its broadest interpretation, this limitation does not require any separation between the layers at all, as long as particle dislodgment is prevented. A distance of zero is sufficient to satisfy this claim limitation. Since Stabile does not teach the dislodgment of the particles from the cavities of the support, the limitations of claim 1 are deemed to be met.

22. Applicant's arguments regarding the combination of Stabile and other references as the bases of proper 103 rejections are based on the premise that Stabile is not a proper 102 reference, a position that has already been addressed and rejected.

Conclusion

Claims 1-36, 39, 173, and 174 are rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kartic Padmanabhan whose telephone number is 703-305-0509. The examiner can normally be reached on M-F (8:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 703-305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-5207 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Kartic Padmanabhan
Patent Examiner
Art Unit 1641

*** KP

March 10, 2003

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

03/10/03